PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:
ANDREW M. PARIAL
KOHN & ASSOCIATES, PLLC
30500 NORTHWESTERN HIGHWAY
SUITE 410
FARMINGTON HILLS, MI 48334

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing (*day/month/year*)	12 JUL 2005
Applicant's or agent's file reference 3087.00017	**FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date (*day/month/year*)
PCT/US05/08973	18 March 2005 (18.03.2005)	19 March 2004 (19.03.2004)

International Patent Classification (IPC) or both national classification and IPC

IPC(7): C12M 1/34, 3/00 and US Cl.: 435/287.2, 435/7.1, 436/518, 422/68.1

Applicant

DETROIT R&D, INC.

1. This opinion contains indications relating to the following items:

☒	Box No. I	Basis of the opinion
☐	Box No. II	Priority
☐	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☒	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☒	Box No. VIII	Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis(b)* that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/ US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Authorized officer Unsu Jung Valerie Bell-Hanus for Telephone No. 571-272-1600

Form PCT/ISA/237 (cover sheet) (January 2004)

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Box No. I Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material

      ☐ a sequence listing

      ☐ table(s) related to the sequence listing

   b. format of material

      ☐ in written format

      ☐ in computer readable form

   c. time of filing/furnishing

      ☐ contained in international application as filed.

      ☐ filed together with the international application in computer readable form.

      ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

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Box No. V Reasoned statement under Rule 43 *bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims 2-4 and 6	YES
	Claims 1, 5, and 7	NO
Inventive step (IS)	Claims NONE	YES
	Claims 1-7	NO
Industrial applicability (IA)	Claims 1-7	YES
	Claims NONE	NO

2. Citations and explanations:

Claims 1, 5, and 7 lack novelty under PCT Article 33(2) as being anticipated by Barry et al. (U.S. PG Pub. No. US 2002/0055186, May 9, 2002).

Barry et al. teaches an antibody microarray (p10, paragraph [0104], lines 1-6) screen comprising a hydrogel substrate (p11, paragraph [0105]), monoclonal and polyclonal antibodies (p9, paragraph [0084], lines 5-8), which are spotted on predetermined positions on the substrate (p10-11, paragraph [0104]) and fluids unprocessed for immunoglobulin isolation (hybridoma, p9, paragraph [0084], lines 5-8), wherein the unprocessed fluids are spotted on the predetermined positions on the substrate.

Claims 2, 3, and 6 lack an inventive step under PCT Article 33(3) as being obvious over Barry et al. (U.S. PG Pub. No. US 2002/0055186, May 9, 2002) in view of Yue et al. (U.S. Patent No. 6,130,077, Oct. 10, 2000).

Barry et al. teaches an antibody microarray screen as discussed above. However, Barry et al. fails to teach the use of the antibody microarray screen to detect proteins selected from the group consisting of drug-metabolizing enzyme and proteins functionally related with the drug-metabolizing enzymes. Yue et al. teaches the method of detecting cytochrome P450, a drug-metabolizing enzyme, using two-site, monoclonal-based immunoassay (column 22, lines 30-40). Cytochrome P450s are associated with inflammation and infection as well as fibrolammelar hepatocellular carcinoma (column 2, lines 15-45) and can be used in the diagnosis treatment, or prevention of cell proliferative, developmental, autoimmune/inflammatory, and metabolic disorders (column 2, lines 55-59). Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to include in the antibody microarray screen of Barry et al. with the cytochrome P450 detection method of Yue et al. in order to utilize in the diagnosis treatment, or prevention of cell proliferative, developmental, autoimmune/inflammatory, and metabolic disorders.

With respect to claim 4, it is well known in the art that cytochrome 450 is an apoptosis-related protein.

With respect to claim 6, Yue et al. teaches a detection method of ELISA, in which labeled secondary immunoglobins are used to detect the presence of an antigen (column 17, lines 59-67).

Claim 4 lack an inventive step under PCT Article 33(3) as being obvious over Barry et al. (U.S. PG Pub. No. US 2002/0055186, May 9, 2002) in view of Yue et al. (U.S. Patent No. 6,130,077, Oct. 10, 2000) in light of Lam et al. (U.S. PG Pub. No. US 2002/0072121 A1, June 13, 2002).

Barry et al. in view of Yue et al. teaches an antibody microarray screen to detect cytochrome P450 as discussed above. However, Barry et al. in view of Yue et al. fails to teach an antibody microarray screen to detect apoptosis-related proteins. Lam et al. teaches that cytochrome P450 gene is capable of killing cells, causing apoptosis, or arresting cells in the cell cycle (p12, paragraph [0138], lines 9-13). Therefore, cytochrome P450 of Yue et al. is an apoptosis related protein.

Claims 1-7 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in the industry.

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Box No. IV Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees the applicant has:
   - ☐ paid additional fees
   - ☐ paid additional fees under protest
   - ☒ not paid additional fees
2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is
   - ☐ complied with
   - ☒ not complied with for the following reasons:

   See the lack of unity section of the International Search Report(Form PCT/ISA/210)

4. Consequently, this opinion has been established in respect of the following parts of the international application:
   - ☐ all parts.
   - ☒ the parts relating to claims Nos. 1-7

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Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the questions whether the claims are fully supported by the description, are made:

Claims 1-7 are objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 6 because claim 1 is indefinite for the following reason(s): In claim 1, purified monoclonal and polyclonal antibodies are used in antibody microarray screen. However, claim 1 also includes fluids unprocessed for immunoglobin isolation, which is in direct contrast to the use of purified immunoglobulins used in the antibody microarray screen.